

REMARKS

General

An Office Action was mailed in the above-captioned application on July 8, 2003. In such Office Action claims 2-8, 10-19, 29-45, 47, 49-52 and 59-63 were pending. Claims 10, 11 and 59-63 were allowed. Claims 13, 16, 33, 36 and 52 were objected to as being dependent upon a rejected base claim. Claims 2-8, 12, 14, 15, 17-19, 29-32, 34, 35, 37-45, 47 and 49-51 were rejected. This Amendment and Remarks document is submitted in response to that Office Action.

Additional claims 64-68 have been added in the application.

Allowed Claims and Claim Objections

Applicant acknowledges with thanks the Examiner's determination that Claims 10, 11 and 59-63 are allowed.

Claims 13, 16, 33, 36 and 52 have been objected to as being dependent upon a rejected base claim. However, the Examiner has stated that these claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. These claims have been rewritten in independent form in accordance with the Examiner's suggestion. In addition, claims 17 and 19 have been amended to depend from amended claim 16. Claims 17 and 19 specify the method used to distinguish the separated extraction probes and are allowable for the same reasons as claim 16. Thus, the Applicant submits that these amendments place Claims 13, 16, 17, 19, 33, 36 and 52 in condition for allowance.

Claims Rejections – 35 USC § 102

Pending claims 2-6, 7, 8, 12, 15, 29-32, 37-45, 47 and 49 were rejected by the Examiner under 35 USC § 102(b) as being anticipated by U.S. Patent No. 5,279,742 to Markell et al. ("Markell et al."). Applicant does not acquiesce in the Examiner's determination that the pending claims are anticipated; however, in the interest of expediting prosecution, these claims have been cancelled without prejudice. Applicant reserves the right to pursue the subject matter of these claims in a continuing application.

Claims Rejections – 35 USC § 103

Pending claims 17-19, 34, 50 and 51 were rejected by the Examiner under 35 USC § 103(a) as being unpatentable over Markell et al. in view of U.S. Patent No. 5,766,962 to Childs et al. Applicant does not acquiesce in the Examiner's determination that the pending claims are obvious; however, in the interest of expediting prosecution, these claims have been cancelled without prejudice. Applicant reserves the right to pursue the subject matter of these claims in a continuing application.

New Claims

New claims 64-68 have been added. The claims are similar to amended claims 1-6 and 9 that were introduced in Applicant's Amendment A (June 19, 2002), rejected in the subsequent Office Action (October 4, 2002), and were ultimately cancelled by Applicant in its Amendment Under 37 CFR §1.116 (January 29, 2003) after a telephone interview with the Examiner that took place on January 28, 2003. New claims 64-68 are drafted to address the Examiner's previously expressed concerns and are patentable over the prior art.

In certain preferred embodiments, the methods of the invention involve the use of a freestanding nanoparticle having a composition that varies along its length. See, e.g., page 16, lines 24-26; page 21, lines 14-16; page 22, lines 19-20; and FIGS. 1-4. The meaning of the term "freestanding" is described on page 25, lines 5-12 of the present application:

"By 'freestanding' it is meant that nanoparticle solid supports that are produced by some form of deposition or growth within a template have been released from the template. Such particles are typically freely dispensable in a liquid and not permanently associated with a stationary phase. Nanoparticles that are not produced by some form of deposition or growth within a template (e.g., self-assembled nanobarcodes) may be considered freestanding even though they have not been released from a template. The term "freestanding" does not imply that such nanoparticles must be in solution (although they may be) or that the particles can not be bound to, incorporated in, or part of a macrostructure."

Thus, as described in the present application, freestanding particles may be, but are not necessarily, (i) freely dispensable in a liquid, (ii) in solution, (iv) permanently associated with a stationary phase, and/or (iv) bound to, incorporated in, or part of a macrostructure. Indeed, the present application specifically describes a variety of such embodiments. In

addition to requiring that the freestanding particle have a composition that varies along its length, new claims 64-68 require both that the freestanding particle is in solution with the sample, and is not bound to, incorporated in, or part of a macrostructure. Support for these limitations is provided, for example, at page 25, lines 10-12; page 8, lines 22-25; and page 32, lines 12-19.

A. *New Claims 64-68 Are Patentable Over Markell et al.*

Markell et al. does not disclose a particle having a composition that varies along its length. Nor does Markell et al. disclose a freestanding particle that is in solution with the sample and is not bound to, incorporated in, or part of a macrostructure. Not only are the particles of the composite structures in Markell et al. contained within the bounds of a disk, the particles are physically immobilized within the disk's fiber matrix. As Markell et al. states, "[i]n such a structure almost all of the particles are separate one from another and each is isolated in a cage that that restrains the particle on all sides by a fibrillated mesh of PTFE microfibers" (col. 8, lines 62-66; emphasis added).

By contrast, as claimed in new claims 64-68, the freestanding particles of the present invention "may be introduced into the sample where they can independently assort in three-dimensions," allowing the extraction phase associated with each particle to contact and interact with analytes present in the sample (page 10, lines 4-7). The use of such particles provides advantages over extraction probes arranged in planar configuration, such as in an array or disk. For example, the extraction may be performed in smaller volumes of sample (see page 11, line 29 – page 12, line 3), and because the extraction phase and the sample are both mobile, equilibration time is shortened as "encounters between [the extraction phase and the sample] occur more frequently and the capture of analyte molecules is more rapid" (page 32, lines 14-17).

There would be no motivation to free the sorbent particles of Markell et al. from their "PTFE cages" because it is properties of the PTFE-particulate composite structure that are responsible for the purported advantages such as strength, self-support, uniform porosity and void volume, uniform distribution of particulate, and convenience (see, e.g., col. 8, lines 55-65). In addition, Markell et al. states that "particles in the PTFE fibrillated matrix provide superior separatory capabilities" over particles not in the matrix (col. 3, lines 55-65). In addition, Markell et al. states that it is advantageous to "stack" disks that contain

different particulates so as to have different selectivities for different contaminants. By separately eluting disks and by using alternate stacking orders, additional information about the types of compounds in each eluting fraction can be obtained (col. 14, lines 29-36; Example 2). These advantages are possible only because the different particles are embedded components of a specific disk that can be separately manipulated and identified. Freeing the particles from their PTFE cages would eliminate these advantages because the particles could not be separately manipulated or identified. Significantly, Markell et al. does not disclose or suggest a means to manipulate (e.g., recover the particles from solution or prevent them from being swept away with the sample flow) or to identify particles other than by their physical association with the disk in which they are embedded.

Applicant therefore submits that amended claims 64-68 are patentable over Markell et al.

B. New Claims 64-68 Are Patentable Over Michael et al.

Michael et al., “Randomly Ordered Addressable High-Density Optical Sensor Arrays,” Anal. Chem. 70:1242-1248 (1998) (“Michael et al.”) does not disclose a freestanding particle having a composition that varies along its length. Nor does Michael et al. disclose a freestanding particle that is in solution with the sample and is not bound to, incorporated in, or part of a macrostructure. Rather, the microbeads in Michael et al. are immobilized in a planar array.

Before being contacted with the sample, the encoded beads of Michael et al. are immobilized by random distribution into wells of a chemically etched optical imaging fiber surface (see, e.g., Michael et al. at FIG. 3). In the series of experiments disclosed in Michael et al., the resulting sensor array was exposed to six different solutions and “neither loss nor rearrangement of the microspheres was observed” (page 1247, first full paragraph). Indeed, Michael et al. states that the microwell “entraps” the microspheres (see page 1247, first full paragraph). Michael et al. does not disclose or suggest a means for ejecting the particles from the surface of the sensor array, and it is clear that a particle must be immobilized on the array to be read.

Applicant therefore submits that amended claims 64-68 are patentable over Michael et al.

C. New Claims 64-68 Are Patentable Over Watkins et al.

U.S. Patent No. 6,280,618 issued to Watkins et al. (“Watkins et al.”) discloses a method for performing multiplexed assays to detect various analytes in a biological sample by using a plurality of magnetically responsive microparticles coupled to assay reagents. The microparticles are classified into groups based on a “differentiation parameter” which allows the groups of microparticles to be distinguished from one another. Each microparticle group carries an assay reagent distinct from the assay reagents of particles in other groups.

Watkins does not disclose a freestanding particle having a composition that varies along its length. Rather, Watkins et al. teaches particles formed from a polymeric material, see col. 4, line 66 – col. 5, line 17, and manufactured by standard emulsion polymerization techniques, see col. 5, lines 44-52). Indeed, Watkins et al. teaches the differentiation of the particles using bulk characteristics of the particles, such as size, fluorescence and light scattering/emission. Thus, there would be no point to using a freestanding particle having a composition that varies along its length in the method of Watkins et al.

Applicant therefore submits that amended claims 64-68 are patentable over Watkins et al.

Conclusion

Applicant believes that the pending claims are in condition for allowance. Thus, Applicant requests that the Examiner reconsider the application and issue a Notice of Allowance in the next Office Action. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested.

The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

Date: December 8, 2003



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